prediction process do not account for the multitude of differences between rodents and humans. In addition, Shelby pointed out that some computer predictions were not subjected to review by human experts at the end of the analyses, and called for "one more loop through the human mind" before results are offered as predictions.

Two challenges presented at the workshop were how to deal with equivocal results in rodent cancer bioassays when assessing their predictions and the question of how carcinogenic potency can be predicted. Workshop participants noted that confirmation of their predictions depend on the rodent bioassay, which has some limitations. Because concordance between rat and mouse bioassays is only about 70%, this might represent an upper limit for extrapolating from rodent carcinogens to human carcinogens. In considering the limitations of the predictive process, Ashby said "Although we have had successes, there is a limit to how far such methods can be refined."

At the end of the workshop, Bernard Schwetz, acting director of the Environmental Toxicology Program at NIEHS, indicated that a variety of prediction methods were under consideration as aids for prioritizing chemicals for rodent carcinogenicity bioassays. A list of chemicals currently being tested in rodent bioassays was distributed, and participants were invited to use this list to further develop their prediction methods. Participants proposed that a similar workshop in about 3 years to evaluate results of new predictions and to review progress in the development of prediction methods.

NTP Announces Study Results for Six Chemicals

The National Toxicology Program presented six technical reports in its ongoing series of toxicology and carcinogenesis studies of selected chemicals at the semiannual public peer review meeting June 22 at NIEHS. Each report involves a series of studies in which male and female rats and mice are given a range of doses of the chemical for 14 days, 13 weeks, and then 2 years. In each study extensive histopathologic diagnoses are performed on all tissue systems, and growth patterns, blood chemistry, urinalysis, and genetic toxicity are evaluated.

Methylphenidate is the active ingredient of Ritalin, a drug used in the treatment of narcolepsy and attention-deficient hyperactivity disorders. In both short-term and two-year studies in mice, the liver was the primary target of toxicity. The incidences of liver tumors were significantly elevated in male and female mice receiving the drug for two years in the feed at doses 5- to 50-fold greater than human doses (on a body weight basis). Similar studies in rats showed no evidence of carcinogenic activity.

Tricresyl phosphate is an organophosphate plasticizer widely used in vinyl plastics and as a flame retardant in hydraulic fluids. When given at concentrations in the feed of up to 300 parts per million (ppm) for rats or 250 ppm for mice, tricresyl phosphate showed no evidence of carcinogenic activity.

4,4'-Thiobis(6-t-butyl-m-cresol) is used as an antioxidant in the rubber and plastics industry and as a stabilizer in polyethylene and polyolefin packaging materials for foods. The chemical did not induce tumors at any site when given at concentrations up to 2500 ppm in the feed for male and female rats or 1000 ppm for male and female mice.

Barium chloride is used in the manufacture of pigments, glass, and ceramics, as a flux in the manufacture of magnesium metal, a lubricating oil additive, and in aluminum refining, leather tanning, photographic paper, and water softening. There was no evidence of carcinogenic activity in male or female rats or mice given feed containing up to 2500 ppm barium chloride for 2 years.

Hexachlorocyclopentadiene (HCCP) is a chemical intermediate used in the manufacture of flame retardants, resins, and pesticides. All rats and mice exposed to atmospheres containing 1 ppm or more of HCCP died within 1 to 5 weeks. Rats exposed to 0.2 ppm HCCP for 2 years developed pigmentation of the epithelial lining of the airways, and mice similarly exposed developed suppurative inflammation of the nose and lungs. Tumors were not produced by exposure at these concentrations.

p-Nitrobenzoic acid is used in organic synthesis, in the manufacture of pesticides, dyes, explosives, and solvents, and as a reagent for alkaloids and thorium. When given at doses up to 5000 ppm in the feed for two years, *p*-nitrobenzoic acid caused increases in clitoral gland tumors in female rats, but decreased incidences of leukemia in male and female rats. Mice were relatively unaffected by the chemical.

Copies of NTP reports are available from NTP Central Data Management, NIEHS, PO Box 12233, Research Triangle Park, NC 27709 USA.

"Predicting Chemical Carcinogenesis in Rodents" Scientific Program Committee (left to right) Joseph Wachsman, Stanley Stasiewicz, John Ashby, Raymond Tennant, Michael Shelby, Judson Spalding, and Douglas Bristol

Casida Receives International Wolf Prize

John E. Casida, who has been a grantee of the NIEHS since 1966, received the international Wolf Foundation Prize for Agriculture. The prize was presented in May by President Ezer Weizman of Israel at the Knesset (parliament) building in Jerusalem. Casida has been on the faculty of the University of California at Berkeley for almost 30 years, where he is a professor of entomology and director of the pesticide chemistry and toxicology laboratory, as well as principal investigator for an NIEHS program project.